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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,648	02/05/2001	Toshiaki Takezawa	202785US0X	3290

22850 7590 06/26/2002

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EXAMINER
MARVICH, MARIA

ART UNIT	PAPER NUMBER
1636	3

DATE MAILED: 06/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/775,648	Applicant(s) TAKEZAWA ET AL.	
	Examiner Maria B. Marvich	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

Claim Objections

Claims 4, 5, 6, 9 and 10 are objected to under 37 CFR 1.75(c) as being in improper form should refer to other claims in the alternative only and because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites a "cell incorporated type three-dimensionally reconstructed tissue" which is a broad, undefined term for which no description in the specification is provided.

Use of the phrase "to induce adhesion and three dimensional growth of the fertilized ovum" is unclear. It is not clear how it is or what induces adhesion and three-dimensional

growth. Redrafting the claims to read "for the purpose of adhesion and three dimensional growth of the fertilized ovum" would be remedial.

Use of the phrase "co-culturing" is unclear. It is not clear with what the fertilized ovum is being **co**-cultured.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification provides support for a carrier characterized in that cells of the cell incorporated type three-dimensional reconstructed tissue are derived from epithelial and stromal endometrial cells from a bovine uterus (page 18, line 9-16), it does not provide support for cell incorporated type three-dimensional reconstructed tissue in which the carrier is derived from any of cells, tissue or organs from any animal. The specification provides support for the use of collagen type I but not for a carrier that contains an extracellular matrix. As well, the specification provides an enabling disclosure for the use of a mesh network composed of gauze or cotton but does not provide support for the use of any natural or synthetic thread in the mesh network that is bioabsorptive. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat.

App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) Unpredictability of the art. This invention recites a carrier for the co-culturing of a fertilized ovum of an animal. The invention recites a carrier characterized by cells or tissue or organ, an extracellular matrix and a mesh network that induces adhesion and growth of a three-dimensional fertilized ovum. Said carrier adds to the prior art of ovum development in which only two-dimensionally proliferated blastulas had been generated. The establishment of three-dimensional ovums was not high art at the time of invention. To date "coaxing cells to form tissues in a reliable manner is the quintessential engineering design problem that must be accomplished under the classical engineering constraints of reliability, cost, government regulation and societal acceptance" (Griffith **et al**, page 1009). Tissue engineering still remains highly unpredictable by any method.

In its broadest sense, the invention reads on a carrier for the development of ovums that have entered the gastrula or neurula stage and hence have an early embryo-like structure (page 4, line 2-3) for in vitro fertilization purposes. This is a non-tested art with a high degree of unpredictability. The claimed invention particularly has a high degree of unpredictability due to the many parameters recited in the claims that had not been addressed.

Cells used in the carrier can be from any cell, tissue or organ from any animal. The ability to grow cells, tissues or organs from any animal is an unpredictable art. The development of primary cells is an art that involves growing in culture cells that are derived from an organ. This alone is a difficult task with few sources capable of consistently and reliably providing cells in culture. Needless to say the use of tissues and organs in culture is rarely accomplished. For

the carrier, these cells, tissues and organs will be used to create an environment for the growth of a fertilized ovum. Cells in culture secrete growth factors and other signals that could adversely affect the growth of the ovum and adherence such that embodiments of the invention such as adhesion and growth are not possible. Cells, organs and tissues may also contain pathogens that would be deleterious to the ovum. Therefore, defined cells with tested applicability to the carriers function are not provided for in the invention.

Similarly, the content of the extracellular matrix (ecm) used in a carrier has essential properties that affect the growth of cells. As described in Naughton **et al**., even the requirement for the type of collagen used varies tissue to tissue. For example, for hematopoietic cells, collagen types III, IV and I in a ratio of 6:3:1 is required while for skin cultures type I and III are required. It is unpredictable that any type of ecm or ecm component will allow for the specialized growth of a fertilized ovum (page 15 lines 48-67).

Use of "mesh" is recited with only gauze and cotton disclosed as potential candidates. Gauze alone is exemplified. Several other natural and synthetic compounds considered usable are providing in the specification such as nylon, acryl and polyester. It is unpredictable that these or any natural or synthetic mesh will provide the proper environment for effective use of the carrier. For example it has been reported that certain materials such as nylon and polystyrene are substrates for cellular substrate (Naughton **et al**.).

2) State of the art. Bioengineered tissues and organs are currently under development using specifically defined polymers for multiple uses from multiple groups. There has been no development of carriers or scaffolds or polymers for the growth of fertilized ovum in vitro.

3) Number of working examples. The specification provides by way of example of claimed invention the development of a carrier comprised of bovine endometrial cells and collagen and incubated with a fertilized ovum from bovine. The adhesion and growth of said ovum was monitored plus and minus gauze as a mesh network.

4) Amount of guidance provided by applicants. Guidance provided by the applicants does not provide for growth conditions, growth characteristics or the effect of different cells, organs and tissues on ovum development. As well, only guidance as to the density and thread thickness 10-100 μm in diameter is provided for the characteristics required for the mesh network but no guidance is provided for characteristics required such as the ability of cells to attach, pretreatment. The exemplary method provided is solely for the generation of a carrier from endometrial bovine cells and collagen that has been "gelated". The additional components for the development of a carrier listed are untested in the instant application and in the art. No guidance is given for the criteria for the choice of mesh like structures. It would require undue experimentation to determine which mesh like structures would function in the carrier given the unpredictability of the art as described above.

5) Nature of invention. The invention recites a carrier for the growth of a fertilized ovum in vitro such that it can develop into a three dimensional structure. This invention utilizes tissue engineering and in vitro fertilization techniques and requires a firm knowledge of animal and cell culture techniques.

6) Level of skill in the art. The level of skill in the art covering this invention is developing at the time of invention. Tissue engineering from which the skills are derived is in the inventive stages with much manpower and interest in its development. Therefore, the skills required to develop

the techniques of the invention are increasingly available. Although the skills for use in the field of in vitro fertilization are not.

7) Scope of the invention. This invention has a broad scope in that it recites development of a carrier comprised of any animal cell, tissue or organ in combination with any mesh like structure for the development of a carrier for the growth of any type of fertilized ovum.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue experimentation and excessive experimentation in order to practice the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucell, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kay Pinkney, whose telephone number is (703) 305-3553.

Maria B Marvich, PhD
Examiner
Art Unit 1636

June 25, 2002

DAVID GUZO
PRIMARY EXAMINER